## REMARKS

Claims 1 and 4-22 are pending in the subject application.

### I. Rejection of Claims 1, 5-10, 14 and 16-18 Under 35 U.S.C. § 102(b) Over Smith et al.

Claims 1, 5-10, 14 and 16-18 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Smith et al. The Examiner asserts that Smith teaches all of the elements of the claimed process, including binding of nucleic acids to a silica based or coated porous matrix. Applicants respectfully disagree.

Claim 1 recites that the target DNA binds directly to a porous matrix consisting of a material based on silica or a silica coated material. The Office Action appears to equate the porous silica-based matrix of the present invention with the solid matrix plus ion exchange material disclosed by Smith et al. The term "silica-based matrix" as used in the present claims is a term of art indicating a solid matrix consisting of materials based on silica, such as glass, for example, which is distinct from an ion exchange matrix as taught by Smith et al. In fact, Smith et al. teach that a "silica based matrix" component like that used in the present invention is used in combination with an ion exchange matrix. See col. 9:32 - 10:30. Thus, Smith et al. provides evidence that the term "silica based matrix" as used herein does not include materials that are not based on silica, such as the ligands taught by Smith et al. Thus, the prior art cited in the Office Action actually teaches that the claimed invention does not include non-silica based materials in the solid matrix to which the nucleic acids bind.

Smith teaches use of an ion exchange matrix attached to a porous or nonporous silica-based matrix support, and teaches that the target nucleic acid attaches to the ion exchange matrix, not the silica based support, establishing an indirect binding of the DNA to the support matrix. Thus, Smith does not teach or suggest the claimed invention.

The Office Action finds that the present claims do not require that the DNA binds directly to the SiO groups of the silica based materials and therefore, makes a correlation between Applicants' claims to direct binding to the solid porous silica based matrix and Smith's use of ion exchange matrices attached to the solid (optionally silica based) support matrix. This correlation has no basis in fact. The fact that the present claims do not specify the molecular binding responsible for the direct binding to the porous silica-based matrix is of no consequence since the claims require that the binding be directly to the silica-based solid matrix and the specification makes clear that the silica-based matrix does not contain non-silica based components. Recitation of how direct binding is accomplished is not required for patentability. The fact is, the present inventors' have discovered that there is no need to modify the surface of a silica-based or silica coated porous matrix to include an ion exchange matrix, for example, in order to capture the filtered DNA in the absence of a chaotropic agent and/or alcohol.

Smith et al. expressly teaches the addition of functional groups to the surface of the solid matrix, *e.g.* , multiple ion exchange matrices attached to a silica based matrix, to capture filtered DNA, thereby indirectly binding the DNA to the solid matrix *via* non-silica-based materials. Thus, Smith et al. does not teach all of the elements of the present claims and does not suggest the claimed invention.

Accordingly, the rejection of claims 1, 5-10, 14 and 16-18 under 35 U.S.C. § 102(b) as allegedly being anticipated by Smith et al. is respectfully traversed.

## II. Rejection of Claim 4 and 19-22 Under 35 U.S.C. § 103(a) Over Smith et al. and Colpan

Claims 4 and 19-22 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentably obvious over Smith et al. in view of Colpan. Smith is applied as above and Colpan is relied on as teaching a method for isolation of genomic DNA having a size in the range of from 1 to 50kb

using an alternative-form of silica-based material as a filter. The Office Action concludes therefore, that it would have been obvious to one of ordinary skill in the art to have used the filter matrices of Smith in the arrangement of Colpan.

Applicants respectfully disagree.

As discussed above, the present invention is based in part on the binding of nucleic acids directly to the silica based or coated porous matrix used in the claimed filtering process, whereas Smith et al. bind nucleic acids to a pH dependent ion exchange matrix which is bound to a solid silica based support. The teachings of Smith et al. demonstrate that the term "silica based-matrix" does not include ligands or other non-silica based materials. Thus, Smith et al. do not teach or suggest binding of nucleic acids directly to a silica-based or coated support and thus, even if one of skill in the art were to use the arrangement suggested by Colpan, the result would not be the present invention. In fact, a reading of Smith et al. as a whole makes it abundantly clear that indirect binding to ion exchange resins that are a separate entity from a silica-based matrix is the essence of the invention disclosed by Smith et al.

Colpan merely teaches certain of the structural features used in the present invention for the isolation of plasmid and genomic DNA, but does not disclose or suggest general binding conditions for DNA. There is no general disclosure for determining the binding conditions for nucleic acids, but instead, Colpan teaches this aspect of the disclosed method through specific examples. In each instance where genomic DNA is isolated, Colpan teaches that the cells are lysed in the presence of guanidinium (See Examples 10 and 11). Only in those examples where plasmid DNA is isolated is it disclosed that binding is carried out in the absence of chaotropic agents. Thus, Colpan does not suggest direct binding of genomic DNA in the absence of a chaotropic agent and only by improperly picking and choosing elements from one example and

applying them to another example has a generalized teaching of binding conditions been derived from the disclosure of Colpan.

Thus, the combination of Colpan and Smith et al. fails to disclose or suggest the present invention. First, Smith et al. teaches the use of an ion exchange matrix for indirectly binding the nucleic acids to the porous/non-porous silica based solid support matrix after disrupting the cells and does not disclose or suggest binding directly to a support matrix consisting of a silica based or coated mattrix material. Second, Colpan teaches use of guanidine-HCl in each instance where genomic DNA is the target of the isolation procedure. Thus, even if one were to combine the two cited references in the manner suggested by the Examiner, the result would not be the present invention where genomic DNA is released from cells in the absence of a chaotropic agent and captured by direct binding to a silica based or coated porous matrix.

Accordingly, the rejection of claims 4 and 9-22 under 35 U.S.C. § 103(a) over Smith et al. in combination with Colpan is respectfully traversed.

## III. Rejection of Claims 11-13 Under 35 U.S.C. § 103(a) Over Smith et al.

Claims 11-13 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentably obvious over Smith et al. The Office Action finds that it would have been obvious to use filters with different pore sizes in Smith's filters to enable capture of genomic DNA. The Office Action concludes, therefore, that the claimed invention would have been obvious to one of skill in the art.

Applicants respectfully disagree.

As discussed above, Smith et al. does not disclose a filter system that binds DNA directly to a silica-based matrix. Instead, Smith utilizes an ion exchange ligand attached to a silica-based support such as a silica bead. There is no teaching or suggestion that direct binding to the porous

silica-based matrix can replace use of ion exchange resins. Thus, regardless of the size of the pores in the solid matrix, the invention of Smith et al. does not render the claimed invention obvious.

Accordingly, the rejection of claims 11-13 under 35 U.S.C. § 103(a) over Smith et al. is respectfully traversed.

## IV. Rejection of Claims 11-13 Under 35 U.S.C. § 103(a) Over Smith et al.

Claims 11-13 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentably obvious over Smith et al. The Office Action finds that it would have been *prima facie* obvious to have used filters with different pore sizes in the method of Smith et al. and finds that use of different pore sizes is mere optimization.

Applicant respectfully disagrees.

As noted above, Smith et al. does not teach the direct binding of DNA from a cell lysate to a silica-based or silica coated porous matrix as required by claims 11-13. In fact, Smith et al. expressly disclose that binding of nucleic acids is *via* an indirect linkage using ion exchange matrices attached to the surface of a solid porous or non-porous support, such as a silica-based support. There clearly is no suggestion of direct binding of DNA to a porous filter in the cited reference.

Moreover, Smith et al. teach that the solid support of the ion exchange matrix can be either porous or non-porous. When a porous support is used, the pores are only of sufficient size to enable the DNA to enter the particle so that it can be bound by the ion exchange matrix. Thus, there is no motivation to modify the pore size of the solid support used in the Smith et al. method. Smith et al. fails to disclose or suggest the claimed invention and "mere optimization"

of the pore sizes used in Smith et al. would not have led the skilled practitioner to the claimed invention.

Accordingly, the rejection of claims 11-13 under 35 U.S.C. § 103(a) over Smith et al. is respectfully traversed.

## V. Rejection of Claim 15 Under 35 U.S.C. § 103(a) Over Smith et al. and Heid et al.

Claim 15 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentably obvious over Smith et al. in view of Heid et al. Smith et al. is applied as above and for teaching amplification of isolated DNA; Heid is relied on as teaching quantitative real-time PCR on human genomic DNA. The Office Action concludes, therefore, that it would have been *prima facie* obvious to one of ordinary skill in the art to have applied real-time PCR to analyze the genomic DNA isolated by the method of Smith et al.

Applicants respectfully disagree.

The present invention differs from and is not rendered obvious by the teachings of Smith et al., alone or in combination with Heid et al. As discussed above, Smith et al. teaches use of a solid support porous matrix to which are attached pH dependent ion exchanges matrixes which bind nucleic acids from a cell lysate. The nucleic acid is not bound directly to the porous matrix as in the present invention. Heid et al. does not cure this deficiency in the primary reference.

Heid et al. merely teaches a method of carrying out quantitative real-time PCR. This reference is silent as to how the DNA used in the PCR assay is isolated. As such, the combination of cited prior art fails to suggest the claimed invention in which DNA, which is isolated using a silica based or silica coated porous matrix with specified pore sizes to directly

bind genomic DNA in the absence of alcohol or chaotropic agents, is used as a template for real time PCR.

It is respectfully submitted that the rejection of claim 15 under 35 U.S.C. § 103(a) over Smith et al. in view of Heid et al. is respectfully traversed.

It is further submitted that the present application is in condition for allowance, an early notification thereof being earnestly solicited.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

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